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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,851	09/09/1999	EDWARD M SELLERS	064658.0129	8120

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BERESKIN AND PARR
40 KING STREET WEST
BOX 401
TORONTO, ON M5H 3Y2
CANADA

EXAMINER	
JAGOE, DONNA A	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/214,851	SELLERS ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20,23,24,27,28 and 39-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20,23,24,27,28 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 19, 20, 23, 24, 27, 28 and 39-41 are pending in this application.

The indicated allowability of claims 19, 20, 23, 24, 27, 28 and 39-41 is withdrawn in view of the newly discovered reference(s). Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 27 contains the term "antimycotic" in the list of CYP2A6 inhibitors. Upon inspection of the specification for guidance, it is found that what is included is "imidazole antimycotics". Not any and all antimycotics. The following precedent is believed relevant to the instant case. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed.Cir.1997), *cert. denied,* 523 U.S. 1089, 118 S.Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties,

"not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed.Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia,* "functional characteristics *when coupled with a known or disclosed correlation between function and structure* ...." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d, 316, 1324-25 (Fed. Cir. 2002) (quoting Guidelines, 66 Fed.Reg. at 1106 (emphasis added)). Moreover, although Eli Lilly and Enzo were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. Univ. of Rochester v. G.D. Searle & Co., 249 F. Supp.2d 216, 225 (W.D.N.Y. 2003).

Applying the reasoning of the above-cited case law to the facts at hand, the instant specification fails to provide an adequate written description for all antimycotic agents to be included in the group of substances that inhibit CYP2A6. The specification describes only a limited number of suitable antimycotics, which are characterized having an imidazole structure. See page 10, first paragraph of the specification. No other detailed, relevant identifying characteristics are specified which would adequately describe suitable antimycotic agent other than the imidazole type structure. Also see Genentech, Inc. v. Novo Nordisk, 108 F.3d 1361, 1366, 42 U.S.P.Q.2d (BNA) 1001, 1005 (Fed. Cir. 1997) (clarifying that the patent monopoly is given in exchange for

enabling disclosure, "not for vague intimations of general ideas that may or may not be workable"); see also Brenner v. Manson, 383 U.S. 519, 536, 148 U.S.P.Q. (BNA) 689, 696 (1966) ("[A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Removal of the comma between the words antimycotics and imidazole (as in claims 19 and 23) would obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19, 20, 23, 24, 27, 28 and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19, 23 and 27 are drawn to a method of enhancing inhibition of nicotine metabolism, a composition for regulating metabolism of nicotine to cotinine and a method for treating a condition requiring regulation of nicotine metabolism comprising administering to the individual an effective amount of a substance which selectively inhibits CYP2A6 and an effective amount of an inhibitor of CYP2A6. In a search for clarification in the instant specification, there is nothing that was found regarding the difference between a substance which selectively inhibits CYP2A6 and an effective amount of an inhibitor of CYP2A6. It is noted that the specification teaches a combination of a CYP2A6 inhibitor and a substance that inhibits transcription/translation of the gene encoding CYP2A6, however it is unclear to the examiner what the

difference would be in an agent that selectively inhibits CYP2A6 and an inhibitor of CYP2A6. If there is a difference, it is unclear what portion of the CYP2A6 enzyme that the substance would target in its selection.

The term "enhancing" in claim 19 is a relative term which renders the claim indefinite. The term "enhancing" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since no guidance is provided as to how "unenhanced" the nicotine metabolism can be and still fall within the scope of the instantly claimed subject matter as circumscribed by the term "enhancing", the metes and bounds of the term are not clear, making it impossible to ascertain with reasonable precision when that term is infringed and when it is not.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte*

Hasche, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 19 and 23 recites the broad recitation imidazole antimycotics, and the claim also recites miconazole which is the narrower statement of the range/limitation since miconazole is an imidazole antimicotic. This leaves one to wonder whether the imidazole antimicotics are limited to miconazole or if it is merely exemplary of the remainder of the claim, and therefore not required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Vinals et al. U.S. Patent No. 3,977,418.

Vinals et al. teach a composition comprising nicotine and coumarin (a substance that inhibits CYP2A6), which would inherently regulate the metabolism of nicotine to cotinine. It is noted that the reference does not teach that the composition can be used in the manner instantly claimed, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural

difference, thus the intended use is not limiting. Since the coumarin and nicotine are present in the composition of the patent, they are capable of performing the intended use of regulating metabolism of nicotine to cotinine, then it meets the claim.

Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Choudhury et al. Cancer Letters (1995).

The claim is drawn to a pharmaceutical composition comprising N-nitrosodiethylamine, N-nitrosodimethylamine or a mixture thereof. Choudhury et al. teach a composition comprising N-nitrosodiethylamine (NDEA) administered to rats (see abstract). It is noted that the reference does not teach that the composition can be used in the manner instantly claimed, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting. Since the NDEA is present in the composition, it is capable of performing the intended use of regulating the metabolism of nicotine to cotinine.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19, 20, 27, 28 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over (U) Berkman et al. Biochemical Pharmacology, (1995) in view of (V) Seaton et al. Pharmac. Ther. 1993. and (W) Draper et al. Arch Biochem Biophys (1997) Berkman et al. teach that CYP2A6 is the primary enzyme that transforms (*S*)-nicotine to (*S*) nicotine $\Delta^{1'5'}$-iminium ion which is converted to (*S*) cotinine by the action of an exogenously added aldehyde oxidase (page 565, column 2, 2nd paragraph bridging to page 566, first paragraph). The formation of (*S*)-cotinine is strongly dependent on the

previous drug administration history of each subject, and among the highest rates for (*S*)-cotinine formation at low concentration correlated well with immunoreactivity for cytochrome P450 2A6 (see abstract). The in vitro/in vivo correlation of the results suggests that the low amount of (*S*)-nicotine N-1'-oxygenation and the large amount of (*S*)-cotinine formed in human smokers are determined primarily by the kinetic properties of the human monooxygenase enzyme systems. It doesn't teach that the CYP2A6 enzyme enhanced inhibition of nicotine metabolism. It teaches that in the presence of CYP2A6, lots of (*S*)-cotinine was formed. Seaton et al. teach that there are many variables to the metabolism of nicotine in a human. It teaches that Phenobarbital, an inducer of CYP450 enzymes induces not only metabolism of nicotine to cotinine, but also metabolism of cotinine to secondary metabolites (page 472 2nd paragraph). Conversely cimetidine, an agent that inhibits the CYP450 enzymes (page 472, 4th paragraph) decreased rates of nicotine metabolism so that twice as much nicotine was excreted unchanged in urine of Macaques (page 473 1st paragraph). Regarding the method for treatment of a condition requiring the regulation of nicotine metabolism to cotinine wherein the condition is dependent on tobacco use, Seaton et al. teach that chronic ethanol administration produces inductive effects of the CYP450 enzymes and induction of nicotine metabolism after chronic ethanol administration resulted in decreased plasma nicotine concentrations (increased metabolism) and might explain the increased urge to smoke cigarettes sometimes associated with heavy alcohol consumption. It would have been made obvious to one of ordinary skill in art at the time it was made to inhibit the CYP2A6 enzyme to inhibit metabolism of nicotine since

Berkman et al. teach that CYP2A6 is the primary enzyme that transforms (*S*)-nicotine to (*S*) nicotine $\Delta^{1'5'}$-iminium ion which is converted to (*S*)-cotinine. It does not teach the specific agents that inhibit the CYP2A6 enzymes, however, Draper et al. teach that inhibitors of CYP2A6 include clotrimazole, diethyldithiocarbamate, ellipticine, ketoconazole, 8-methoxypsoralen (methoxsalen), 4-methylpyrazole, metyrapone, miconazole, alpha naphthoflavone, nicotine p-nitrophenol and tranylcypromine (see abstract). Seaton et al. teaches inhibitors of CYP450 decrease nicotine metabolism (chronic ethanol administration) and agents that induce CYP450 increase nicotine metabolism (Phenobarbital). Combined with the teaching of Berkman et al. that CYP2A6 is the primary enzyme that transforms (*S*)-nicotine to (*S*) nicotine $\Delta^{1'5'}$-iminium ion which is converted to (*S*) cotinine one would have been motivated to employ inhibitors of CYP2A6 to inhibit nicotine metabolism.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

August 31, 2006

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER